Marcaine® 0.5% with epinephrine 1:200,000 injection (as bitartrate) (bupivacaine hydrochloride and epinephrine injection, USP)

Rx only

THIS SOLUTION IS INTENDED FOR DENTAL USE

DESCRIPTION

Bupivacaine hydrochloride is (±)-1-Butyl-2’, 6’-piperidoxylidide monohydrochloride, monohydrate, a white crystalline powder that is freely soluble in 95 percent ethanol, soluble in water, and slightly soluble in chloroform or acetone. It has the following structural formula:

\[
\text{CH}_3 \quad \text{CONH} \quad \text{HCl} \quad \text{H}_2\text{O}
\]

Molecular Weight - 342.90

\[
\text{C}_{18} \text{H}_{28} \text{N}_2\text{O} \quad \text{HCl} \quad \text{H}_2\text{O}
\]

Molecular Weight - 183.20

Epinephrine is (±)-3, 4-Dihydroxy-α-(methylamino)-methyl) benzyl alcohol. It has the following structural formula:

\[
\text{CH}_3 \quad \text{OH} \quad \text{O} \quad \text{CH}_2\text{NHCH}_3 \quad \text{H}
\]

CONTRAINDICATIONS

Marcaine® 0.5% with epinephrine 1:200,000 injection, is contraindicated in patients with a known hypersensitivity to it or to any local anesthetic agent of the amide type or to other components of bupivacaine solutions.

INDICATIONS AND USAGE

Marcaine® 0.5% with epinephrine 1:200,000 injection is indicated for the production of local anesthesia for dental procedures by infiltration injection or nerve block in adults.

Marcaine® 0.5% with epinephrine 1:200,000 injection is not recommended for children.

ADVERSE REACTIONS

PRECAUTIONS

See also SIDE EFFECTS and PRECAUTIONS. DELAY IN PROPER MANAGEMENT OF DOSE-RELATED TOXICITY, UNDERVENTILATION FROM THE BLOCK TO BE EMPLOYED, AND THEN ONLY AFTER INSURING THE IMMEDIATE AVAILABILITY OF OXYGEN, OTHER RESUSCITATIVE DRUGS, CARDIOPULMONARY RESUSCITATIVE EQUIPMENT, AND THE PERSONAL RESOURCES NEEDED FOR PROPER MANAGEMENT OF TOXIC REACTIONS AND RELATED EMERGENCIES. (See also ADVERSE REACTIONS and PRECAUTIONS.) DELAY IN PROPER MANAGEMENT OF DOSE-RELATED TOXICITY, UNDERVENTILATION FROM ANY CAUSE, AND/OR ALTERED SENSITIVITY MAY LEAD TO THE DEVELOPMENT OF ACIDOSIS, CARDIAC ARREST AND, POSSIBLY, DEATH.

Small doses of local anesthetics injected into the head and neck area, as small as sixteen to eighteen milligrams, may produce adverse reactions similar to systemic toxicity seen with unintentional intravascular injections of larger doses. Confusion, convulsions, respiratory depression, and/or respiratory arrest, cardiovascular stimulation or depression and cardiac arrest have been reported. Reactions resulting in fatalities have occurred on rare occasions. In a few cases, recovery has been difficult or impossible despite apparently adequate preparation and appropriate management. These reactions may be due to intra-arterial injection of the local anesthetic with retrograde flow to the cerebral circulation. Patients receiving these blocks should have their circulation and respiration monitored and be constantly observed. Resuscitative equipment and personnel for treating adverse reactions should be immediately available. Dosage recommendations should not be exceeded (see DOSAGE AND ADMINISTRATION).

It is essential that aspiration for blood or cerebrospinal fluid (where applicable) be done prior to injecting any local anesthetic, both the original dose and all subsequent doses, to avoid intravascular injection. However, a negative aspiration does not ensure against an intravascular injection.

Reactions resulting in fatality have occurred on rare occasions with the use of local anesthetics, even in the absence of a history of hypersensitivity. This condition, which contains a vasconstrictor, should be used with extreme caution for patients whose medical history and physical examination suggest the existence of hypertension, arteriosclerotic heart disease, cerebrovascular insufficiency, heart block, thyrotoxicosis and diabetes, etc., as well as patients receiving drugs likely to produce alterations in blood pressure.

Methemoglobinemia: Cases of methemoglobinemia have been reported in association with local anesthetic use. Although all patients are at risk for methemoglobinemia, patients with glucose-6-phosphate dehydrogenase deficiency, congenital or idiopathic methemoglobinemia, cardiac or pulmonary compromise, infants under 6 months of age, and concurrent exposure to oxidizing agents or their metabolites are more susceptible to developing clinical manifestations of the condition. If local anesthetics must be used in these patients, close monitoring for symptoms and signs of methemoglobinemia is recommended.

Signs of methemoglobinemia may occur immediately or may be delayed some hours after exposure, and are characterized by cyanotic skin discoloration and/or abnormal coloration of the blood. Methemoglobin levels may continue to rise; therefore, immediate treatment is required to avert more serious central nervous system and cardiovascular adverse effects, including seizures, coma, arrhythmias, and death. Discontinue Marcaine® and any other oxidizing agents. Depending on the severity of the signs and symptoms, patients may respond to supportive care, i.e., oxygen therapy, hydration. A more severe clinical presentation may require treatment with methylene blue, exchange transfusion, or hyperbaric oxygen.

Marcaine® 0.5% with epinephrine 1:200,000 injection or other vasoconstrictors should not be used concomitantly with ergot-type oxytocic drugs, because a severe persistent hypertension may occur. Likewise, solutions of bupivacaine containing a vasoconstrictor, such as epinephrine, should be used with extreme caution in patients receiving monoamine oxidase inhibitors (MAOI) or antidepressants of the triphenyl or imipramine types, because severe prolonged hypertension may result.

Until further experience is gained in children younger than 12 years, administration of bupivacaine in this age group is not recommended.

Effects of bupivacaine on the cardiovascular system are discussed in detail in the information on the effects of the amide-type local anesthetics, which have an ester linkage.

CLINICAL PHARMACOLOGY

Bupivacaine stabilizes the neuronal membrane and prevents the initiation and transmission of nerve impulses, thereby effecting local anesthesia. The onset of action following dental injections is usually 2 to 10 minutes and anesthesia may last two or three times longer than lidocaine and mepivacaine for dental use, in many patients up to 7 hours. The duration of anesthetic effect is prolonged by the addition of epinephrine 1:200,000.

It has also been noted that there is a period of analgesia that persists after the return of sensation, during which time the need for strong analgesic is reduced.

Following systemic absorption, local anesthetics can produce central nervous system stimulation, depression, or both. Apparent central stimulation is manifested as restlessness, tremors and shivering progressing to convulsions, followed by depression and coma progressing ultimately to respiratory arrest. However, the local anesthetics have a primary depressant effect on the medulla and on higher centers. The depressed stage may occur without a prior excited state.

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Molecular Weight - 183.20

\[
\text{C}_9 \text{H}_3 \text{NO}_3
\]
Marcaine® 0.5% with epinephrine 1:200,000 injection (NDC 0362-0557-05) is available in cartons containing 5 blisters of 10 X 1.8 mL dental cartridges.

Information for Patients/Patient Counseling Information: When used concurrently with other agents that may affect cardiovascular function or systemic absorption, the combined action of both agents upon the myocardium, the concentration and volume of vasoconstrictor used, and the time since injection, when applicable, should be taken into account.

Marcaine® 0.5% with epinephrine 1:200,000 injection should be used cautiously in persons with known drug allergies or sensitivities, particularly to the amide-type local anesthetics. Serious dose-related cardiac arrhythmias may occur if preparations containing a vasoconstrictor such as epinephrine are employed in patients during or following the administration of chloroform, halothane, cyclopropane, trichlorethylen, or other related agents. In deciding whether to use these products concurrently in the same patient, the combined action of both agents upon the myocardium, the concentration and volume of vasoconstrictor used, and the time since injection, when applicable, should be taken into account.

Drug Interactions: See WARNINGS concerning solutions containing a vasoconstrictor. If sedatives are employed to reduce patient apprehension, use reduced doses, since local anesthetic agents, like sedatives, are central nervous system depressants which in combination may have an additive effect. Marcaine® 0.5% with epinephrine 1:200,000 injection should be used cautiously in persons with known drug allergies or sensitivities, particularly to the amide-type local anesthetics. Serious dose-related cardiac arrhythmias may occur if preparations containing a vasoconstrictor such as epinephrine are employed in patients during or following the administration of chloroform, halothane, cyclopropane, trichlorethylen, or other related agents. In deciding whether to use these products concurrently in the same patient, the combined action of both agents upon the myocardium, the concentration and volume of vasoconstrictor used, and the time since injection, when applicable, should be taken into account.

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